AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

What is claimed is:

1. (Currently amended). A non-naturally occurring nucleic acid molecule encoding a polypeptide comprising a first carboxy-terminal portion of a split intein (C-intein), a second amino-terminal portion of a split intein (N-intein), and a target peptide ~~interposed between the first portion of a split intein and the second portion of a split intein~~ flanked on one end with the carboxy-terminal portion of a split intein (C-intein) and on its other end with the amino-terminal portion of a split intein (N-intein); wherein expression of the nucleic acid molecule in a host system produces the polypeptide in a form selected from the group consisting of: (a) a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide, and (b) a splicing intermediate of a cyclized form of the target peptide.

2. (Original). The non-naturally occurring nucleic acid molecule of claim 1, wherein the polypeptide is a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide.

3. (Original). The non-naturally occurring nucleic acid molecule of claim 1, wherein the polypeptide is a splicing intermediate of a cyclized form of the target peptide.

4. (Currently amended). The non-naturally occurring nucleic acid molecule of claim 1, wherein both the first portion of a split intein and the second portion of a split intein ~~correspond to~~ is a naturally-occurring split intein.

5. (Currently Amended). The non-naturally occurring nucleic acid molecule of claim 4, wherein both the first portion of a split intein and the second portion of a split intein ~~are correspond to~~ is an Ssp DnaE.

6. (Currently Amended). The non-naturally occurring nucleic acid molecule of claim 1, wherein at least one of the first portion of a split intein and the second portion of a split intein ~~correspond to~~ is a non-naturally occurring split intein.

7. (Previously presented). The non-naturally occurring nucleic acid molecule of claim 6, wherein the non-naturally occurring split intein is selected from the group consisting of RecA, DnaB, Psp, Pol-I, and Pfu inteins.

8. (Currently Amended). The non-naturally occurring nucleic acid molecule of claim 1 , wherein both the first portion of a split intein and the second portion of a split intein ~~correspond to~~ is a non-naturally occurring split intein.

9. (Original). The non-naturally occurring nucleic acid molecule of claim 3, wherein the splicing intermediate is an active intein intermediate.

10. (Original). The non-naturally occurring nucleic acid molecule of claim 3, wherein the splicing intermediate is a thioester intermediate.

11. (Original). The non-naturally occurring nucleic acid molecule of claim 3, wherein the splicing intermediate is a lariat intermediate.

12. (Withdrawn). A non-naturally occurring nucleic acid molecule encoding a polypeptide comprising a first portion of a split intein, a second portion of a split intein, a third portion of a split intein, and fourth portion of a split intein, wherein a first target

peptide is interposed between the first portion of a split intein and the second portion of a split intein, and a second target peptide is interposed between the third portion of a split intein and the fourth portion of a split intein.

13. (Withdrawn). The non-naturally occurring nucleic acid molecule of claim 12 wherein the first portion of a split intein is complementary to the third portion of a split intein but not complementary to the second portion of a split intein, and the second portion of a split intein is complementary to the fourth portion of a split intein but not complementary to the third portion of a split intein.

14. (Currently amended). An expression vector comprising a nucleic acid molecule that encodes a polypeptide comprising a first carboxy-terminal portion of a split intein (C-intein), a second amino-terminal portion of a split intein (N-intein), and a target peptide ~~interposed between the first portion of a split intein and the second portion of a split intein~~ flanked on one end with the carboxy-terminal portion of a split intein (C-intein) and on its other end with the amino-terminal portion of a split intein (N-intein), wherein expression of the nucleic acid molecule in a host system produces the polypeptide in a form selected from the group consisting of: (a) a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide, and (b) a splicing intermediate of a cyclized form of the target peptide.

15. (Original). The expression vector of claim 14, wherein the polypeptide is a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide.

16. (Original). The expression vector of claim 14, wherein the polypeptide is a splicing intermediate of a cyclized form of the target peptide.

17. (Original). The expression vector of claim 15, wherein the nucleic acid molecule further comprises a regulatory sequence that facilitates expression of the polypeptide in the host system.

18. (Original). The expression vector of claim 14, wherein the nucleic acid molecule further comprises a nucleotide sequence that encodes a peptide that facilitates screening of the cyclized form of the target peptide for a particular characteristic.

19. (Original). The expression vector of claim 14, wherein the nucleic acid molecule further comprises a nucleotide sequence that encodes a peptide that facilitates purifying the cyclized form of the target peptide from the host system.

20. (Original). The expression vector of claim 14, wherein the target peptide has a first end fused to the first portion of a split intein and a second end fused to the second portion of a split intein.

21. (Original). The expression vector of claim 14, wherein both the first portion of a split intein and the second portion of a split intein are derived from a naturally-occurring split intein.

22. (Original). The expression vector of claim 21, wherein both the first portion of a split intein and the second portion of a split intein are derived from Ssp DnaE.

23. (Original). The expression vector of claim 14, wherein at least one of the first portion of a split intein and the second portion of a split intein is derived from a non-naturally occurring split intein.

24. (Original). The expression vector of claim 23, wherein the non-naturally occurring split intein is derived from the group consisting of RecA, DnaB, Psp Pol-I, and Pfu inteins.

25. (Original). The expression vector of claim 14, wherein both the first portion of a split intein and the second portion of a split intein are derived from a non-naturally occurring split intein.

26. (Original). The expression vector of claim 16, wherein the splicing intermediate is a active intein intermediate.

27. (Original). The expression vector of claim 16, wherein the splicing intermediate is a thioester intermediate.

28. (Original). The expression vector of claim 16, wherein the splicing intermediate is a lariat intermediate.

29. (Original). The expression vector of claim 14, wherein the host system comprises a prokaryotic cell.

30. (Original). The expression vector of claim 29, wherein the prokaryotic cell is a bacterium.

31. (Original). The expression vector of claim 30, wherein the bacterium is *Escherichia coli*.

32. (Original). The expression vector of claim 14, wherein the host system comprises a eukaryotic cell.

33. (Original). The expression vector of claim 32 , wherein the eukaryotic cell is a yeast.

34. (Original). The expression vector of claim 33, wherein the eukaryotic cell is a mammalian cell.

35. (Original). The expression vector of claim 14, wherein the host system comprises an archaebacterium.

36. (Original). The expression vector of claim 14, wherein the host system comprises a plant cell.

37. (Original). The expression vector of claim 14, wherein the vector is a plasmid.

38. (Original). The expression vector of claim 14, wherein the vector is a bacteriophage.

39. (Original). The expression vector of claim 14, wherein the vector is a virus.

40. (Original). The expression vector of claim 14, wherein the vector is a linear nucleic acid molecule.

41. (Withdrawn). A substantially pure polypeptide comprising a first portion of a split intein, a second portion of a split intein, and a target peptide interposed between the first portion of a split intein and the second portion of a split intein, wherein the polypeptide is selected from the group consisting of: (a) a polypeptide that spontaneously

splices in the host system to yield a cyclized form of the target peptide, and (b) a splicing intermediate of a cyclized form of the target peptide.

42. (Withdrawn). The polypeptide of claim 41, wherein the polypeptide is a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide.

43. (Withdrawn). The polypeptide of claim 41, wherein the polypeptide is a splicing intermediate of a cyclized form of the target peptide.

44. (Withdrawn). The polypeptide of claim 41, wherein the target peptide has a first end fused to the first portion of a split intein and a second end fused to the second portion of a split intein.

45. (Withdrawn). The polypeptide of claim 41, wherein both the first portion of a split intein and the second portion of a split intein are derived from a naturally-occurring split intein.

46. (Withdrawn). The polypeptide of claim 45, wherein both the first portion of a split intein and the second portion of a split intein are derived from Ssp DnaE.

47. (Withdrawn). The polypeptide of claim 41, wherein at least one of the first portion of a split intein and the second portion of a split intein is derived from a non-naturally occurring split intein.

48. (Withdrawn). The polypeptide of claim 47, wherein the non-naturally occurring split intein is derived from the group consisting of RecA, DnaB, Psp Pol-I, and Pfu inteins.

49. (Withdrawn). The polypeptide of claim 41, wherein both the first portion of a split intein and the second portion of a split intein are derived from a non-naturally occurring split intein.

50. (Withdrawn). The polypeptide of claim 43, wherein the splicing intermediate is a active intein intermediate.

51. (Withdrawn). The polypeptide of claim 43, wherein the splicing intermediate is a thioester intermediate.

52. (Withdrawn). The polypeptide of claim 43, wherein the splicing intermediate is a lariat intermediate.

53. (Currently amended). A host system comprising a non-naturally occurring nucleic acid molecule encoding a polypeptide comprising a first carboxy-terminal portion of a split intein (C-intein), a second amino-terminal portion of a split intein (N-intein), and a target peptide ~~interposed between the first portion of a split intein and the second portion of a split intein~~ flanked on one end with the carboxy-terminal portion of a split intein (C-intein) and on its other end with the amino-terminal portion of a split intein (N-intein); wherein expression of the nucleic acid molecule in the host system produces the polypeptide in a form selected from the group consisting of: (a) a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide, and (b) a splicing intermediate of a cyclized form of the target peptide.

54. (Original). The host system of claim 53, wherein the polypeptide is a polypeptide that spontaneously splices in the host system to yield a cyclized form of the target peptide.

55. (Original). The host system of claim 53, wherein the polypeptide is a splicing intermediate of a cyclized form of the target peptide.

56. (Original). The host system of claim 53, wherein the host system comprises a prokaryote.

57. (Original). The host system of claim 56, wherein the prokaryote is a bacterium.

58. (Original). The host system of claim 53, wherein the host system comprises an archaebacterium.

59. (Original). The host system of claim 53, wherein the host system comprises a eukaryote.

60. (Original). The host system of claim 59, wherein the eukaryote is a yeast.

61. (Original). The host system of claim 59, wherein the eukaryote is a mammalian cell.

62. (Original). The host system of claim 53, wherein the host system comprises a plant cell.

63. (Original). A method for making a peptide molecule, the method comprising the steps of: providing an isolated nucleic acid molecule that encodes a polypeptide comprising a first portion of a split intein, a second portion of a split intein, and a target peptide interposed between the first portion of a split intein and the second portion of a split intein, wherein expression of the nucleic acid molecule in a host system

produces the peptide molecule in a form selected from the group consisting of: (a) a cyclized form of the target peptide resulting from spontaneously splicing of the polypeptide in the host system, and (b) a splicing intermediate of a cyclized form of the target peptide; providing the host system; introducing the isolated nucleic acid molecule into the host system; and expressing the isolated nucleic acid molecule.

64. (Original). The method of claim 63, wherein the step of expressing the isolated nucleic acid molecule results in production of a polypeptide that spontaneously splices in the host system to yield the cyclized form of the target peptide.

65. (Original). The method of claim 64 further comprising the step of purifying the cyclized form of the target peptide from the host system.

66. (Original). The method of claim 63, wherein the step of expressing the isolated nucleic acid molecule results in production of a splicing intermediate of a cyclized form of the target peptide.

67. (Original). The method of claim 66 further comprising the step of purifying the splicing intermediate of a cyclized form of the target peptide from the host system.

68. (Original). The method of claim 66, wherein the splicing intermediate is an active intein intermediate.

69. (Original). The method of claim 66, wherein the splicing intermediate is a thioester intermediate.

70. (Original). The method of claim 66, wherein the splicing intermediate is a lariat intermediate.

71. (Original). The method of claim 66, further comprising the step of forming the cyclic peptide from the splicing intermediate.

72. (Original). The method of claim 63, wherein the isolated nucleic acid molecule is incorporated into an expression vector that facilitates expression of the isolated nucleic acid molecule in the host system.

73. (Original). The method of claim 72, wherein the expression vector is a plasmid.

74. (Original). The method of claim 72, wherein the expression vector is a bacteriophage.

75. (Original). The method of claim 72, wherein the expression vector is a virus.

76. (Original). The method of claim 63, wherein the host system comprises a prokaryotic cell.

77. (Original). The method of claim 76, wherein the prokaryotic cell is a bacterium.

78. (Original). The method of claim 77, wherein the bacterium is *Escherichia coli*.

79. (Original). The host system of claim 63, wherein the host system comprises an archaebacterium.

80. (Original). The method of claim 63, wherein the host system comprises a eukaryotic cell.

81. (Original). The method of claim 80, wherein the eukaryotic cell is a yeast.

82. (Original). The method of claim 80, wherein the eukaryotic cell is a mammalian cell.

83. (Original). The method of claim 63, wherein the host system comprises a plant cell.

84. (Original). The method of claim 63, wherein the host system comprises an *in vitro* transcription/translation system.

85. (Original). The method of claim 84, wherein the in vitro transcription/translation system comprises a cell lysate.

86. (Original). The method of claim 64, wherein the production of the target peptide in cyclized form occurs in the host system in the absence of an exogenously-added agent.

87. (Original). The method of claim 86, wherein the exogenously-added agent is a protease.

88. (Original). The method of claim 86, wherein the exogenously-added agent is a thiol.

89. (Original). The method of claim 72, wherein the expression vector is inducible.

90. (Withdrawn). A method of preparing a library of peptide molecules, the method comprising the steps of:

providing a plurality of nucleic acid molecules encoding a plurality of target peptides having heterogeneous amino acid sequences;

incorporating each of the plurality of nucleic acid molecules into an expression vector to form a plurality of expression vectors, whereby each of the plurality of nucleic acid molecules is interposed between a nucleic acid molecule encoding a first portion of a split intein and a nucleic acid molecule encoding an second portion of a split intein in each of the formed expression vectors, wherein expression of the expression vectors in a host system results in the production of a plurality of peptide molecules in a form selected from the group consisting of: (a) polypeptides that spontaneously splice in the host system to yield cyclized forms of the target peptides, and (b) splicing intermediates of cyclized forms of the target peptides; and

expressing the expression vectors in the host system.

91. (Withdrawn). The method of claim 90, wherein the plurality of polypeptides are polypeptides that spontaneously splice in the host system to yield cyclized forms of the target peptides.

92. (Withdrawn). The method of claim 90, wherein the plurality of polypeptides are splicing intermediates of cyclized forms of the target peptides

93. (Withdrawn). The method of claim 90, wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced by solid phase synthesis.

94. (Withdrawn). The method of claim 90, wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced using polymerase chain reaction.

95. (Withdrawn). The method of claim 90, wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced by enzymatically digesting a larger nucleic acid molecule.

96. (Withdrawn). The method of claim 95, wherein the larger nucleic acid molecule is derived from an organism.

97. (Withdrawn). The method of claim 90, wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced from a progenitor nucleic acid molecule that has been amplified under conditions which introduce mutations into the progenitor nucleic acid molecule's nucleotide sequence.

98. (Withdrawn). A method of screening a peptide molecule for a predetermined characteristic, the method comprising the steps of: providing a nucleic acid molecule that encodes a polypeptide comprising a first portion of a split intein, a second portion of a split intein, and a target peptide interposed between the first portion of a split intein and the second portion of a split intein, wherein expression of the nucleic acid molecule in a host system produces the peptide molecule in a form selected from the group consisting of: (a) a cyclized form of the target peptide resulting from spontaneously splicing of the polypeptide in the host system, and (b) a splicing intermediate of a cyclized form of the target peptide; providing the host system; introducing the isolated nucleic acid molecule in the host system; placing the host system under conditions that cause the peptide molecule to be produced; and testing the peptide molecule for the predetermined characteristic.

99. (Withdrawn). The method of claim 98, wherein the peptide molecule is a cyclized form of the target peptide.

100. (Withdrawn). The method of claim 98, wherein the peptide molecule is a splicing intermediate of a cyclized form of the target peptide.

101. (Withdrawn). The method of claim 98, wherein the predetermined characteristic comprises the ability to specifically bind a target molecule, and the step of testing the peptide molecule for the predetermined characteristic comprises the steps of (a) contacting the peptide molecule to the target molecule and (b) determining whether the peptide molecule binds to the target molecule.

102. (Withdrawn). The method of claim 101, wherein the step of determining whether the peptide molecule binds to the target molecule is measured by observing a color change.

103. (Withdrawn). The method of claim 101, wherein the step of determining whether the peptide molecule binds to the target molecule is measured by observing a fluorescent signal.

104. (Withdrawn). The method of claim 101, wherein the step of determining whether the peptide molecule binds to the target molecule is measured by analyzing the cell cycle of an organism.

105. (Withdrawn). The method of claim 101, wherein the step of determining whether the peptide molecule binds to the target molecule is measured by analyzing the reproduction of an organism.

106 (Withdrawn). The method of claim 101, wherein the target molecule is a cell-associated molecule.

107. (Withdrawn). The method of claim 106, wherein the cell-associated molecule is a membrane-associated molecule.

108. (Withdrawn). The method of claim 106, wherein the cell-associated molecule is an intracellular molecule.

109. (Withdrawn). The method of claim 108. wherein the intracellular molecule is a nuclear molecule.

110. (Withdrawn). The method of claim 108, wherein the intracellular molecule is an organelle.

111. (Withdrawn). The method of claim 110, wherein the organelle is selected from the group consisting of: mitochondria, lysosomes, endoplasmic reticula, chloroplasts, golgi, and periplasm.

112. (Withdrawn). The method of claim 101, wherein the target molecule is an extracellular molecule.

113. (Withdrawn). The method of claim 98, wherein the predetermined characteristic is the ability to modulate a biochemical reaction, and the step of testing the peptide molecule for the predetermined characteristic comprises the steps of (a) contacting the peptide molecule to a system containing the biochemical reaction and (b) determining whether the peptide molecule modulates the biochemical reaction.

114. (Withdrawn). The method of claim 113, wherein the step of determining whether the peptide molecule modulates the biochemical reaction is measured by observing a color change.

115. (Withdrawn). The method of claim 113, wherein the step of determining whether the peptide molecule modulates the biochemical reaction is measured by observing a fluorescent signal.

116. (Withdrawn). The method of claim 113, wherein the step of determining whether the peptide molecule modulates the biochemical reaction is measured by analyzing the cell cycle of an organism.

117. (Withdrawn). The method of claim 113, wherein the step of determining whether the peptide molecule modulates the biochemical reaction is measured by analyzing the reproduction of an organism.

118. (Withdrawn). The method of claim 113, wherein the biochemical reaction is an a cell associated process.

119. (Withdrawn). The method of claim 118, wherein the biochemical reaction is an intracellular metabolic event.

120. (Withdrawn). The method of claim 118, wherein the biochemical reaction is a membrane-associated event.

121. (Withdrawn). The method of claim 118, wherein the biochemical reaction is a nuclear event.

122 (Withdrawn). The method of claim 113, wherein the biochemical reaction is a extracellular reaction.

123. (Withdrawn). The method of claim 98, wherein the step of testing the peptide molecule for the predetermined characteristic is performed using a hybrid system.

124. (Withdrawn). The method of claim 98, further comprising the step of immobilizing the peptide molecule on a solid phase support.

125. (Withdrawn). A method for purifying a cyclic peptide from a mixture, the method comprising the steps of: providing a mixture containing a splicing intermediate conjugated with an affinity tag; mixing the conjugated splicing intermediate with a solid phase support having a ligand thereon that specifically binds the affinity tag whereby the support becomes specifically bound with the splicing intermediate; washing the support to remove non-specifically bound matter from the support; adding to the support a reagent that makes a cyclic peptide from the splicing intermediate; and eluting the cyclic peptide from the support.

126. (Withdrawn). A method for purifying a cyclic peptide from a mixture, the method comprising the steps of: providing a mixture containing a splicing intermediate conjugated with an affinity tag; mixing the conjugated splicing intermediate with a solid phase support having a ligand thereon that specifically binds the affinity tag whereby the support becomes specifically bound with the splicing intermediate; washing the support to remove non-specifically bound matter from the support; eluting the splicing intermediate from the support; and adding a reagent the eluted splicing intermediate that make a cyclic peptide from the splicing intermediate;

127. (Withdrawn). A method for purifying a target molecule that binds a splicing intermediate from a mixture, the method comprising the steps of: providing a solid phase support having the splicing intermediate specifically bound thereon; contacting the support with the target molecule in the mixture; washing the support to remove non-specifically bound matter from the support; and eluting the target molecule from the support.